```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:36:30 ON 06 JAN 2004

=> fil .bec
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.42       0.42

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS,
       ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 14:37:22 ON 06 JAN 2004
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s dna(w)(pk or activated(w)(protein kinase# or pk))
FILE 'MEDLINE'
        722320 DNA
        140277 PK
        201039 ACTIVATED
       1216566 PROTEIN
        201605 KINASE#
         97422 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
        140277 PK
L1         739 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'SCISEARCH'
        504755 DNA
         17810 PK
        216314 ACTIVATED
       1053206 PROTEIN
        228526 KINASE#
        114268 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
         17810 PK
L2         571 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'LIFESCI'
        238712 DNA
          4435 PK
         75343 ACTIVATED
        422077 "PROTEIN"
         65330 KINASE#
         31903 PROTEIN KINASE#
                 ("PROTEIN"(W)KINASE#)
          4435 PK
L3         355 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'BIOTECHDS'
        108124 DNA
           277 PK
         11211 ACTIVATED
        110468 PROTEIN
          7170 KINASE#
          1368 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
           277 PK
L4           8 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'BIOSIS'
       1010122 DNA
         15310 PK
        232092 ACTIVATED
```

```
       1353191 PROTEIN
        257667 KINASE#
        119347 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
         15310 PK
L5         624 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'EMBASE'
        536832 DNA
        153992 PK
        202593 ACTIVATED
       1184515 "PROTEIN"
        177240 KINASE#
         91455 PROTEIN KINASE#
                 ("PROTEIN"(W)KINASE#)
        153992 PK
L6         517 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'HCAPLUS'
        642331 DNA
         21424 PK
        422678 ACTIVATED
       1580042 PROTEIN
        213660 KINASE#
         99627 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
         21424 PK
L7         588 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'NTIS'
          8662 DNA
           364 PK
          9794 ACTIVATED
         12172 PROTEIN
          1438 KINASE#
           465 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
           364 PK
L8          10 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'ESBIOBASE'
        223714 DNA
          6631 PK
         95120 ACTIVATED
        497449 PROTEIN
         94412 KINASE#
         54819 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
          6631 PK
L9         475 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'BIOTECHNO'
        387475 DNA
          4752 PK
         93104 ACTIVATED
        621717 PROTEIN
         92000 KINASE#
         48594 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
          4752 PK
L10        385 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

FILE 'WPIDS'
         54631 DNA
```

```
          1578 PK
        121408 ACTIVATED
        107940 PROTEIN
          8333 KINASE#
          2305 PROTEIN KINASE#
                 (PROTEIN(W)KINASE#)
          1578 PK
L11         22 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

TOTAL FOR ALL FILES
L12       4294 DNA(W)(PK OR ACTIVATED(W)(PROTEIN KINASE# OR PK))

=> s p53
FILE 'MEDLINE'
L13      30099 P53

FILE 'SCISEARCH'
L14      37717 P53

FILE 'LIFESCI'
L15      10095 P53

FILE 'BIOTECHDS'
L16       1169 P53

FILE 'BIOSIS'
L17      36353 P53

FILE 'EMBASE'
L18      28199 P53

FILE 'HCAPLUS'
L19      25632 P53

FILE 'NTIS'
L20        435 P53

FILE 'ESBIOBASE'
L21      18107 P53

FILE 'BIOTECHNO'
L22      16151 P53

FILE 'WPIDS'
L23       1173 P53

TOTAL FOR ALL FILES
L24     205130 P53

=> s l24(8a)(fragment# or peptide# or portion#)
FILE 'MEDLINE'
        209320 FRAGMENT#
        339672 PEPTIDE#
         88026 PORTION#
L25        542 L13(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'SCISEARCH'
        160671 FRAGMENT#
        250317 PEPTIDE#
         76405 PORTION#
L26        591 L14(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'LIFESCI'
         76035 FRAGMENT#
```

```
         90028 PEPTIDE#
         28527 PORTION#
L27        337 L15(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'BIOTECHDS'
         41282 FRAGMENT#
         26818 PEPTIDE#
          9824 PORTION#
L28         86 L16(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'BIOSIS'
        185594 FRAGMENT#
        298644 PEPTIDE#
        105352 PORTION#
L29        571 L17(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'EMBASE'
        143646 FRAGMENT#
        219600 PEPTIDE#
         80780 PORTION#
L30        580 L18(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'HCAPLUS'
        291572 FRAGMENT#
        386657 PEPTIDE#
        291113 PORTION#
L31        841 L19(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'NTIS'
          7845 FRAGMENT#
          3744 PEPTIDE#
         32701 PORTION#
L32          12 L20(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'ESBIOBASE'
         58150 FRAGMENT#
         96501 PEPTIDE#
         26229 PORTION#
L33        413 L21(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'BIOTECHNO'
         99755 FRAGMENT#
        106710 PEPTIDE#
         25359 PORTION#
L34        479 L22(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

FILE 'WPIDS'
         48363 FRAGMENT#
         42631 PEPTIDE#
       1025841 PORTION#
L35        107 L23(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

TOTAL FOR ALL FILES
L36       4559 L24(8A)(FRAGMENT# OR PEPTIDE# OR PORTION#)

=> s l36 and human
FILE 'MEDLINE'
       8328136 HUMAN
L37         430 L25 AND HUMAN

FILE 'SCISEARCH'
       1076207 HUMAN
L38         337 L26 AND HUMAN
```

```
FILE 'LIFESCI'
       330836 HUMAN
L39       182 L27 AND HUMAN

FILE 'BIOTECHDS'
        60093 HUMAN
L40        55 L28 AND HUMAN

FILE 'BIOSIS'
      6145688 HUMAN
L41       400 L29 AND HUMAN

FILE 'EMBASE'
      4902084 HUMAN
L42       451 L30 AND HUMAN

FILE 'HCAPLUS'
      1215566 HUMAN
L43       521 L31 AND HUMAN

FILE 'NTIS'
        82115 HUMAN
L44         4 L32 AND HUMAN

FILE 'ESBIOBASE'
       377963 HUMAN
L45       213 L33 AND HUMAN

FILE 'BIOTECHNO'
       734173 HUMAN
L46       383 L34 AND HUMAN

FILE 'WPIDS'
       136164 HUMAN
L47        64 L35 AND HUMAN

TOTAL FOR ALL FILES
L48      3040 L36 AND HUMAN

=> s (l12 or l48) and py=<1993 range=2003,
FILE 'MEDLINE'
'2003,' IS NOT A VALID RANGE FOR FILE 'MEDLINE'
SEARCH ENDED BY USER

FILE 'SCISEARCH'
            0 PY=<1993
L49         0 (L2 OR L38) AND PY=<1993

FILE 'LIFESCI'
           63 PY=<1993
L50         0 (L3 OR L39) AND PY=<1993

FILE 'BIOTECHDS'
            1 PY=<1993
                (PY=<1993)
L51         0 (L4 OR L40) AND PY=<1993

FILE 'BIOSIS'
            1 PY=<1993
L52         0 (L5 OR L41) AND PY=<1993

FILE 'EMBASE'
            0 PY=<1993
L53         0 (L6 OR L42) AND PY=<1993
```

```
FILE 'HCAPLUS'
           89 PY=<1993
L54         0 (L7 OR L43) AND PY=<1993

FILE 'NTIS'
          299 PY=<1993
L55         0 (L8 OR L44) AND PY=<1993

FILE 'ESBIOBASE'
            0 PY=<1993
L56         0 (L9 OR L45) AND PY=<1993

FILE 'BIOTECHNO'
       642571 PY=<1993
L57        70 (L10 OR L46) AND PY=<1993

FILE 'WPIDS'
          142 PY=<1993
                (PY=<1993)
L58         0 (L11 OR L47) AND PY=<1993

TOTAL FOR ALL FILES
L59        70 (L12 OR L48) AND PY=<1993

=> fil medli
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    16.50      16.92

FILE 'MEDLINE' ENTERED AT 14:42:27 ON 06 JAN 2004

=> s (l12 or l48) and py=<1993 range=2003000000,
          1763 PY=<1993
L60         0 (L1 OR L37) AND PY=<1993

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.38      17.30

STN INTERNATIONAL LOGOFF AT 14:42:47 ON 06 JAN 2004
```

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	135	dna adj (pk or activated adj (protein adj kinase$1 or pk))	USPAT; US-PGPUB	2004/01/06 10:35
2	L2	43	1 same (substrate$ or peptide$)	USPAT; US-PGPUB	2004/01/06 10:41
3	L3	27	1 same (assay$8 or detect$8 or quantit$8)	USPAT; US-PGPUB	2004/01/06 10:46
4	L5	8136	p53	USPAT; US-PGPUB	2004/01/06 10:49
5	L6	622	5 near6 (fragment$4 or peptide$ or portion$)	USPAT; US-PGPUB	2004/01/06 10:49
6	L7	1213	5 near4 human	USPAT; US-PGPUB	2004/01/06 10:49
7	L8	332	6 and 7	USPAT; US-PGPUB	2004/01/06 10:49
8	L9	651	5 same (phosphorylat$ or kinase$1 or termin$8) same (fragment$4 or peptide$ or portion$)	USPAT; US-PGPUB	2004/01/06 10:50
9	L10	153	8 and 9	USPAT; US-PGPUB	2004/01/06 10:50
10	L11	20	6 and 1	USPAT; US-PGPUB	2004/01/06 11:45

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	135	dna adj (pk or activated adj (protein adj kinase$1 or pk))	USPAT; US-PGPUB	2004/01/06 10:35
2	L2	43	1 same (substrate$ or peptide$)	USPAT; US-PGPUB	2004/01/06 10:41

PGPUB-DOCUMENT-NUMBER: 20040002128

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040002128 A1

TITLE: GFP-based constructs and methods for detecting apoptosis

PUBLICATION-DATE: January 1, 2004

US-CL-CURRENT: 435/23, 530/350

APPL-NO: 10/ 341979

DATE FILED: January 11, 2003

RELATED-US-APPL-DATA:

child 10341979 A1 20030111

parent continuation-in-part-of 09866447 20010524 US PENDING

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
CN	CN 02120427.6	2002CN-CN 02120427.6	May 24, 2002

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This is a continuation-in-part of application Ser. No. 09/866,447 entitled "GFP-based Methods for Detecting Apoptosis" filed on 24 May 2001. Additional priority is claimed from the People's Republic of China Patent Application No. 02120427.6, filed on 24 May 2002.

PGPUB-DOCUMENT-NUMBER: 20030229105

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030229105 A1

TITLE: Treatment of autoimmune disorders

PUBLICATION-DATE: December 11, 2003

US-CL-CURRENT: 514/263.2, 514/263.22 , 514/263.4

APPL-NO: 10/ 153441

DATE FILED: May 21, 2002

PGPUB-DOCUMENT-NUMBER: 20030211548

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030211548 A1

TITLE: Visualization and quantitiation of cellular cytotoxicity using cell-permeable fluorogenic protease substrates and caspase activity indicator markers

PUBLICATION-DATE: November 13, 2003

US-CL-CURRENT: 435/7.2, 435/23 , 435/5

APPL-NO: 10/ 353791

DATE FILED: January 28, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60353712 20020129 US

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to and benefit of U.S. S. No. 60/353,7112, filed on Jan. 29, 2002, which is incorporated herein by reference in its entirety for all purposes.

PGPUB-DOCUMENT-NUMBER: 20030208037

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030208037 A1

TITLE: Novel fluorescence dyes and their applications for whole-cell fluorescence screening assays for caspases, peptidases, proteases and other enzymes and the use thereof

PUBLICATION-DATE: November 6, 2003

US-CL-CURRENT: 530/330, 549/223

APPL-NO: 10/ 138375

DATE FILED: May 6, 2002

RELATED-US-APPL-DATA:

child 10138375 A1 20020506

parent continuation-of 09583225 20000530 US ABANDONED

child 09583225 20000530 US

parent division-of 09357952 19990721 US GRANTED

parent-patent 6248904 US

non-provisional-of-provisional 60093642 19980721 US

PGPUB-DOCUMENT-NUMBER: 20030203407

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030203407 A1

TITLE: Compositions and methods for monitoring the phosphorylation of natural binding partners

PUBLICATION-DATE: October 30, 2003

US-CL-CURRENT: 435/7.1, 530/388.26

APPL-NO: 10/ 382017

DATE FILED: March 5, 2003

RELATED-US-APPL-DATA:

child 10382017 A1 20030305

parent division-of 09511204 20000223 US PENDING

child 09511204 20000223 US

parent continuation-in-part-of 09258981 19990226 US PENDING

PGPUB-DOCUMENT-NUMBER: 20030194749

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030194749 A1

TITLE: Wortmannin derivatives as probes of cellular proteins and processes

PUBLICATION-DATE: October 16, 2003

US-CL-CURRENT: 435/7.1, 435/194 , 514/211.08 , 514/27 , 514/422 , 514/453 , 514/456

APPL-NO: 10/ 368248

DATE FILED: February 18, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60357538 20020215 US

RELATED APPLICATION

[0001] This application claims the benefit of the filing date of U.S. Provisional Application No. 60/357,538, filed Feb. 15, 2002 and entitled "Wortmannin Derivatives as Probes of Cellular Proteins and Processes," by Thomas Wandless and Karlene Cimprich. The entire teachings of the referenced provisional application are incorporated herein by reference.

[0002] Throughout this application, various publications are referenced by author name and publication date. Full citations for those publications may be found at the end of the specification immediately proceeding the claims. The disclosure of all referenced publications is hereby incorporated by reference into this application to describe more fully the art to which this invention pertains.

PGPUB-DOCUMENT-NUMBER: 20030176373

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030176373 A1

TITLE: Agents that modulate DNA-PK activity and methods of use thereof

PUBLICATION-DATE: September 18, 2003

US-CL-CURRENT: 514/44, 435/455 , 435/6

APPL-NO: 09/ 848986

DATE FILED: May 4, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60202274 20000505 US

non-provisional-of-provisional 60262321 20010117 US

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application serial No. 60/202,274, filed May 5, 2000, and U.S. Provisional Application serial No. 60/262,321, filed Jan. 17, 2001, both of which are incorporated by reference herein in their entirety.

PGPUB-DOCUMENT-NUMBER: 20030171429

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030171429 A1

TITLE: Anti-inflammatory and psoriasis treatment and protein kinase inhibition by hydroxyltilbenes and novel stilbene derivatives and analogues

PUBLICATION-DATE: September 11, 2003

US-CL-CURRENT: 514/475, 514/733 , 549/551 , 549/556

APPL-NO: 10/ 148863

DATE FILED: October 28, 2002

PCT-DATA:
APPL-NO: PCT/CA00/01433
DATE-FILED: Dec 6, 2000
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

PGPUB-DOCUMENT-NUMBER: 20030170655

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030170655 A1

TITLE: Mus101 and homologue thereof

PUBLICATION-DATE: September 11, 2003

US-CL-CURRENT: 435/6, 435/320.1 , 435/325 , 435/348 , 435/69.1 , 435/7.1 , 530/350 , 530/388.1 , 536/23.2

APPL-NO: 10/ 168424

DATE FILED: November 13, 2002

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
GB	9930708.4	1999GB-9930708.4	December 24, 1999

PCT-DATA:
APPL-NO: PCT/GB00/04956
DATE-FILED: Dec 21, 2000
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

PGPUB-DOCUMENT-NUMBER: 20030165956

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030165956 A1

TITLE: Electrophoretic assay to predict risk of cancer and the efficacy and toxicity of cancer therapy

PUBLICATION-DATE: September 4, 2003

US-CL-CURRENT: 435/6

APPL-NO: 10/ 351247

DATE FILED: January 24, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60351732 20020125 US

[0001] This application claims priority to co-pending U.S. Provisional Application, Serial No. 60/351,732 filed Jan. 25, 2002. The entire text of the above-referenced disclosure is specifically incorporated herein by reference without disclaimer.

PGPUB-DOCUMENT-NUMBER: 20030162230

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162230 A1

TITLE: Method for quantifying phosphokinase activity on proteins

PUBLICATION-DATE: August 28, 2003

US-CL-CURRENT: 435/7.4

APPL-NO: 09/ 948972

DATE FILED: September 7, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60235620 20000927 US

PGPUB-DOCUMENT-NUMBER: 20030157572

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030157572 A1

TITLE: ATM kinase compositions and methods

PUBLICATION-DATE: August 21, 2003

US-CL-CURRENT: 435/7.2, 435/194 , 435/7.92

APPL-NO: 10/ 351733

DATE FILED: January 24, 2003

RELATED-US-APPL-DATA:

child 10351733 A1 20030124

parent continuation-in-part-of 10307077 20021127 US PENDING

INTRODUCTION

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 10/307,077, filed Nov. 27, 2002 which is incorporated herein by reference in its entirety.

PGPUB-DOCUMENT-NUMBER: 20030129651

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030129651 A1

TITLE: Expression and purification of ATM protein using vaccinia virus

PUBLICATION-DATE: July 10, 2003

US-CL-CURRENT: 435/7.1, 435/320.1 , 435/367 , 435/456 , 435/69.1 , 530/350 , 536/23.2

APPL-NO: 10/ 042775

DATE FILED: January 8, 2002

PGPUB-DOCUMENT-NUMBER: 20030125284

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030125284 A1

TITLE: Agents that modulate DNA-PK activity and methods of use thereof

PUBLICATION-DATE: July 3, 2003

US-CL-CURRENT: 514/44, 435/6

APPL-NO: 10/ 233121

DATE FILED: August 30, 2002

RELATED-US-APPL-DATA:

child 10233121 A1 20020830

parent division-of 09848986 20010504 US PENDING

non-provisional-of-provisional 60202274 20000505 US

non-provisional-of-provisional 60262321 20010117 US

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application serial No. 60/202,274, filed May 5, 2000, and U.S. Provisional Application serial No. 60/262,321, filed Jan. 17, 2001, both of which are incorporated by reference herein in their entirety.

PGPUB-DOCUMENT-NUMBER: 20030124130

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030124130 A1

TITLE: Proteomic analysis of tumors for development of consultative report of therapeutic options

PUBLICATION-DATE: July 3, 2003

US-CL-CURRENT: 424/155.1, 435/7.23 , 702/19

APPL-NO: 10/ 325793

DATE FILED: December 19, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60345309 20020102 US

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 60/345,309, filed Jan. 2, 2002, which is hereby incorporated by reference in its entirety.

US-PAT-NO: 6670144

DOCUMENT-IDENTIFIER: US 6670144 B1

TITLE: Compositions and methods for monitoring the phosphorylation of natural binding partners

DATE-ISSUED: December 30, 2003

US-CL-CURRENT: 435/21, 435/183 , 435/188 , 435/188.5 , 435/194 , 435/7.8 , 435/7.9 , 435/7.91

APPL-NO: 09/ 511204

DATE FILED: February 23, 2000

PARENT-CASE:

This application is a continuation-in-part of application Ser. No. 09/258,981, filed Feb. 26, 1999.

US-PAT-NO: 6656696

DOCUMENT-IDENTIFIER: US 6656696 B2

TITLE: Compositions and methods for monitoring the phosphorylation of natural binding partners

DATE-ISSUED: December 2, 2003

US-CL-CURRENT: 435/7.6, 435/188 , 435/21 , 435/7.1 , 435/7.4 , 435/7.7 , 435/7.71 , 435/7.72 , 435/7.9 , 436/537 , 436/544 , 436/546 , 536/25.32

APPL-NO: 09/ 258981

DATE FILED: February 26, 1999

US-PAT-NO: 6610835

DOCUMENT-IDENTIFIER: US 6610835 B1

TITLE: Sphingolipid derivatives and their methods of use

DATE-ISSUED: August 26, 2003

US-CL-CURRENT: 536/4.1, 536/17.2 , 536/17.9 , 536/18.2

APPL-NO: 09/ 249211

DATE FILED: February 12, 1999

PARENT-CASE:

This application claims priority to U.S. provisional application No. 60/074,536, filed on Feb. 12, 1998.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	135	dna adj (pk or activated adj (protein adj kinase$1 or pk))	USPAT; US-PGPUB	2004/01/06 10:35
2	L2	43	1 same (substrate$ or peptide$)	USPAT; US-PGPUB	2004/01/06 10:41
3	L3	27	1 same (assay$8 or detect$8 or quantit$8)	USPAT; US-PGPUB	2004/01/06 10:46

PGPUB-DOCUMENT-NUMBER: 20040002492

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040002492 A1

TITLE: ATM inhibitors

PUBLICATION-DATE: January 1, 2004

US-CL-CURRENT: 514/225.2, 514/227.8 , 514/231.5 , 514/336 , 514/431 , 514/434 , 514/443 , 544/149 , 544/35 , 544/60 , 546/282.1 , 549/12 , 549/16 , 549/26 , 549/293 , 549/419 , 549/43

APPL-NO: 10/ 373114

DATE FILED: February 24, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60360493 20020228 US

non-provisional-of-provisional 60395884 20020715 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
GB	0204350.3	2002GB-0204350.3	February 25, 2002

PGPUB-DOCUMENT-NUMBER: 20030229105

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030229105 A1

TITLE: Treatment of autoimmune disorders

PUBLICATION-DATE: December 11, 2003

US-CL-CURRENT: 514/263.2, 514/263.22 , 514/263.4

APPL-NO: 10/ 153441

DATE FILED: May 21, 2002

PGPUB-DOCUMENT-NUMBER: 20030211548

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030211548 A1

TITLE: Visualization and quantitiation of cellular cytotoxicity using cell-permeable fluorogenic protease substrates and caspase activity indicator markers

PUBLICATION-DATE: November 13, 2003

US-CL-CURRENT: 435/7.2, 435/23 , 435/5

APPL-NO: 10/ 353791

DATE FILED: January 28, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60353712 20020129 US

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to and benefit of U.S. S. No. 60/353,7112, filed on Jan. 29, 2002, which is incorporated herein by reference in its entirety for all purposes.

PGPUB-DOCUMENT-NUMBER: 20030194749

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030194749 A1

TITLE: Wortmannin derivatives as probes of cellular proteins and processes

PUBLICATION-DATE: October 16, 2003

US-CL-CURRENT: 435/7.1, 435/194 , 514/211.08 , 514/27 , 514/422 , 514/453 , 514/456

APPL-NO: 10/ 368248

DATE FILED: February 18, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60357538 20020215 US

RELATED APPLICATION

[0001] This application claims the benefit of the filing date of U.S. Provisional Application No. 60/357,538, filed Feb. 15, 2002 and entitled "Wortmannin Derivatives as Probes of Cellular Proteins and Processes," by Thomas Wandless and Karlene Cimprich. The entire teachings of the referenced provisional application are incorporated herein by reference.

[0002] Throughout this application, various publications are referenced by author name and publication date. Full citations for those publications may be found at the end of the specification immediately proceeding the claims. The disclosure of all referenced publications is hereby incorporated by reference into this application to describe more fully the art to which this invention pertains.

PGPUB-DOCUMENT-NUMBER: 20030176373

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030176373 A1

TITLE: Agents that modulate DNA-PK activity and methods of use thereof

PUBLICATION-DATE: September 18, 2003

US-CL-CURRENT: 514/44, 435/455 , 435/6

APPL-NO: 09/ 848986

DATE FILED: May 4, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60202274 20000505 US

non-provisional-of-provisional 60262321 20010117 US

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application serial No. 60/202,274, filed May 5, 2000, and U.S. Provisional Application serial No. 60/262,321, filed Jan. 17, 2001, both of which are incorporated by reference herein in their entirety.

PGPUB-DOCUMENT-NUMBER: 20030171429

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030171429 A1

TITLE: Anti-inflammatory and psoriasis treatment and protein kinase inhibition by hydroxyltilbenes and novel stilbene derivatives and analogues

PUBLICATION-DATE: September 11, 2003

US-CL-CURRENT: 514/475, 514/733 , 549/551 , 549/556

APPL-NO: 10/ 148863

DATE FILED: October 28, 2002

PCT-DATA:
APPL-NO: PCT/CA00/01433
DATE-FILED: Dec 6, 2000
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

PGPUB-DOCUMENT-NUMBER: 20030165956

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030165956 A1

TITLE: Electrophoretic assay to predict risk of cancer and the efficacy and toxicity of cancer therapy

PUBLICATION-DATE: September 4, 2003

US-CL-CURRENT: 435/6

APPL-NO: 10/ 351247

DATE FILED: January 24, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60351732 20020125 US

[0001] This application claims priority to co-pending U.S. Provisional Application, Serial No. 60/351,732 filed Jan. 25, 2002. The entire text of the above-referenced disclosure is specifically incorporated herein by reference without disclaimer.

PGPUB-DOCUMENT-NUMBER: 20030125284

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030125284 A1

TITLE: Agents that modulate DNA-PK activity and methods of use thereof

PUBLICATION-DATE: July 3, 2003

US-CL-CURRENT: 514/44, 435/6

APPL-NO: 10/ 233121

DATE FILED: August 30, 2002

RELATED-US-APPL-DATA:

child 10233121 A1 20020830

parent division-of 09848986 20010504 US PENDING

non-provisional-of-provisional 60202274 20000505 US

non-provisional-of-provisional 60262321 20010117 US

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application serial No. 60/202,274, filed May 5, 2000, and U.S. Provisional Application serial No. 60/262,321, filed Jan. 17, 2001, both of which are incorporated by reference herein in their entirety.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	135	dna adj (pk or activated adj (protein adj kinase$1 or pk))	USPAT; US-PGPUB	2004/01/06 10:35
2	L2	43	1 same (substrate$ or peptide$)	USPAT; US-PGPUB	2004/01/06 10:41
3	L3	27	1 same (assay$8 or detect$8 or quantit$8)	USPAT; US-PGPUB	2004/01/06 10:46
4	L5	8136	p53	USPAT; US-PGPUB	2004/01/06 10:49
5	L6	622	5 near6 (fragment$4 or peptide$ or portion$)	USPAT; US-PGPUB	2004/01/06 10:49
6	L7	1213	5 near4 human	USPAT; US-PGPUB	2004/01/06 10:49
7	L8	332	6 and 7	USPAT; US-PGPUB	2004/01/06 10:49
8	L9	651	5 same (phosphorylat$ or kinase$1 or termin$8) same (fragment$4 or peptide$ or portion$)	USPAT; US-PGPUB	2004/01/06 10:50
9	L10	153	8 and 9	USPAT; US-PGPUB	2004/01/06 10:50

PGPUB-DOCUMENT-NUMBER: 20030228675

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030228675 A1

TITLE: ATM related kinase ATX, nucleic acids encoding same and methods of use

PUBLICATION-DATE: December 11, 2003

US-CL-CURRENT: 435/199, 435/320.1 , 435/325 , 435/69.1 , 514/263.3 , 536/23.2

APPL-NO: 10/ 165216

DATE FILED: June 6, 2002

PGPUB-DOCUMENT-NUMBER: 20030228627

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030228627 A1

TITLE: Assay for p53 function in cells

PUBLICATION-DATE: December 11, 2003

US-CL-CURRENT: 435/7.1, 435/7.23

APPL-NO: 10/ 397131

DATE FILED: March 24, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60366897 20020322 US

RELATED APPLICATIONS

[0001] This applications claims the benefit of priority under 35 U.S.C. 119(e) of U.S. Provisional Application No. 60/366,897, filed Mar. 22, 2002.

PGPUB-DOCUMENT-NUMBER: 20030225025

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030225025 A1

TITLE: MDA-7 proteins and methods of use thereof

PUBLICATION-DATE: December 4, 2003

US-CL-CURRENT: 514/44, 435/6

APPL-NO: 10/ 417827

DATE FILED: April 17, 2003

RELATED-US-APPL-DATA:

child 10417827 A1 20030417

parent continuation-of 09221268 19981223 US PENDING

child 09221268 19981223 US

parent continuation-of 08316537 19940930 US GRANTED

parent-patent 6051376 US

child 08316537 19940930 US

parent continuation-in-part-of 08143576 19931027 US GRANTED

parent-patent 5643761 US

[0001] This application is a continuation-in-part of U.S. application Ser. No. 08/143,576 filed Oct. 27, 1993, the contents of which are hereby incorporated by reference.

PGPUB-DOCUMENT-NUMBER: 20030186861

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030186861 A1

TITLE: HAUSP-p53 interaction and uses thereof

PUBLICATION-DATE: October 2, 2003

US-CL-CURRENT: 514/12, 435/6 , 435/7.23

APPL-NO: 10/ 113732

DATE FILED: March 30, 2002

PGPUB-DOCUMENT-NUMBER: 20030176343

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030176343 A1

TITLE: Diagnostics and therapeutic uses of topors

PUBLICATION-DATE: September 18, 2003

US-CL-CURRENT: 514/12, 424/93.2 , 435/6 , 435/7.23 , 514/44 , 530/388.26

APPL-NO: 10/ 339924

DATE FILED: January 9, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60346953 20020109 US

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present utility patent application claims priority to provisional patent application 60/346,953 (Rubin, et al.), filed Jan. 9, 2002, which is incorporated by reference in its entirety herein.

PGPUB-DOCUMENT-NUMBER: 20030175862

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175862 A1

TITLE: Engineered open reading frame for p53

PUBLICATION-DATE: September 18, 2003

US-CL-CURRENT: 435/69.1, 435/189 , 435/252.3 , 435/320.1 , 536/23.2

APPL-NO: 10/ 077176

DATE FILED: February 19, 2002

PGPUB-DOCUMENT-NUMBER: 20030171537

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030171537 A1

TITLE: Peptides and peptidomimetics with structural similarity to human p53 that activate p53 function

PUBLICATION-DATE: September 11, 2003

US-CL-CURRENT: 530/324, 435/6

APPL-NO: 09/ 829922

DATE FILED: April 11, 2001

RELATED-US-APPL-DATA:

child 09829922 A1 20010411

parent division-of 08894327 19971204 US GRANTED

parent-patent 6245886 US

child 08894327 19971204 US

parent a-371-of-international PCT/US96/01535 19960216 WO PENDING

child 08894327 19971204 US

parent a-371-of-international 08392542 19950216 US GRANTED

parent-patent 6169073 US

PGPUB-DOCUMENT-NUMBER: 20030166674

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030166674 A1

TITLE: 1-Azabicyclo[2.2.2]octan-3-one derivatives and maleimide derivatives and their use for treating cancer tumors

PUBLICATION-DATE: September 4, 2003

US-CL-CURRENT: 514/304, 514/424

APPL-NO: 10/ 381011

DATE FILED: March 20, 2003

PCT-DATA:
APPL-NO: PCT/SE01/02008
DATE-FILED: Sep 19, 2001
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

PGPUB-DOCUMENT-NUMBER: 20030149261

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030149261 A1

TITLE: Sir2 products and activities

PUBLICATION-DATE: August 7, 2003

US-CL-CURRENT: 536/26.1, 435/90 , 544/244

APPL-NO: 10/ 301514

DATE FILED: November 21, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60331919 20011121 US

PGPUB-DOCUMENT-NUMBER: 20030149038

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030149038 A1

TITLE: Alpha-helix mimicry by a class of organic molecules

PUBLICATION-DATE: August 7, 2003

US-CL-CURRENT: 514/234.5, 514/242 , 514/248 , 514/249 , 514/252.02
, 514/263.22 , 514/307 , 514/314 , 514/332 , 514/333
, 544/112 , 544/115 , 544/117 , 544/236 , 544/238 , 544/277
, 544/350 , 544/353 , 544/405 , 546/148 , 546/167 , 546/256

APPL-NO: 10/ 293179

DATE FILED: November 12, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60339239 20011109 US

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. S No. 60/339,239 filed Nov. 9, 2001, which is incorporated herein by reference.

PGPUB-DOCUMENT-NUMBER: 20030133971

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030133971 A1

TITLE: Senescent cell-derived inhibitors of DNA synthesis

PUBLICATION-DATE: July 17, 2003

US-CL-CURRENT: 424/450, 435/458 , 514/12 , 514/44

APPL-NO: 10/ 008960

DATE FILED: December 7, 2001

RELATED-US-APPL-DATA:

child 10008960 A1 20011207

parent continuation-of 08327874 19941024 US GRANTED

parent-patent 6372249 US

child 08327874 19941024 US

parent continuation-in-part-of PCT/US94/09700 19940826 US PENDING

child PCT/US94/09700 19940826 US

parent continuation-in-part-of 08274535 19940713 US ABANDONED

child 08274535 19940713 US

parent continuation-in-part-of 08229420 19940415 US ABANDONED

child 08229420 19940415 US

parent continuation-in-part-of 08203535 19940225 US ABANDONED

child 08203535 19940225 US

parent continuation-in-part-of 08153564 19931117 US ABANDONED

child 08153564 19931117 US

parent continuation-in-part-of 08113372 19930830 US ABANDONED

child 08113372 19930830 US

parent continuation-in-part-of 07970462 19921102 US GRANTED

parent-patent 5302706 US

child 08113372 19930830 US

parent continuation-in-part-of 08160814 19940103 US GRANTED

parent-patent 5424400 US

child 08113372 19930830 US

parent continuation-in-part-of 08268439 19940630 US ABANDONED

child 08268439 19940630 US

parent continuation-in-part-of 07808523 19911216 US ABANDONED

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of PCT US94/09700 (filed Aug. 26, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/274,535 (filed Jul. 13, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/229,420 (filed Apr. 15, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/203,535 (filed Feb. 25, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/153,564 (filed Nov. 17, 1993) which is a continuation-in-part of U.S. patent application Ser. No. 08/113,372 (filed Aug. 30, 1993) which is a continuation-in-part of U.S. patent application Ser. No. 07/970,462 (filed Nov. 2, 1992, and issued as U.S. Pat. No. 5,302,706 on Apr. 12, 1994); and divisional U.S. patent application Ser. No. 08/160,814 (filed Jan. 3, 1994, pending) and Ser. No. 08/268,439 (filed Jun. 30, 1994); all of which Applications are continuations-in-part of U.S. patent application Ser. No. 07/808,523 (filed Dec. 16, 1991, now abandoned).

PGPUB-DOCUMENT-NUMBER: 20030124557

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030124557 A1

TITLE: Peptides and peptidomimetics with structural similarity to human p53 that activate p53 function

PUBLICATION-DATE: July 3, 2003

US-CL-CURRENT: 435/6, 435/189 , 435/320.1 , 435/325 , 435/69.1 , 435/7.23 , 530/317 , 536/23.2

APPL-NO: 10/ 160290

DATE FILED: June 4, 2002

RELATED-US-APPL-DATA:

child 10160290 A1 20020604

parent division-of 09685027 20001010 US GRANTED

parent-patent 6420118 US

child 09685027 20001010 US

parent division-of 08392542 19950216 US GRANTED

parent-patent 6169073 US

PGPUB-DOCUMENT-NUMBER: 20030124101

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030124101 A1

TITLE: Sir2alpha-based therapeutic and prophylactic methods

PUBLICATION-DATE: July 3, 2003

US-CL-CURRENT: 424/93.21, 514/355 , 514/44 , 514/720

APPL-NO: 10/ 172706

DATE FILED: June 14, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60298506 20010615 US

[0001] This application claims the benefit of U.S. Provisional Application No. 60/298,506, filed Jun. 15, 2001, the contents of which are hereby incorporated by reference into this application.

PGPUB-DOCUMENT-NUMBER: 20030109518

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109518 A1

TITLE: Substituted 1,4-benzodiazepines and uses thereof

PUBLICATION-DATE: June 12, 2003

US-CL-CURRENT: 514/221, 514/220 , 540/495 , 540/504 , 540/505

APPL-NO: 10/ 292876

DATE FILED: November 13, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60331235 20011113 US

[0001] This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional Application No. 60/331,235, filed Nov. 13, 2001, which is fully incorporated by reference herein.

US-PAT-NO: 6653465

DOCUMENT-IDENTIFIER: US 6653465 B2

TITLE: Spliced gene of KSHV / HHV8, its promoter and monoclonal antibodies specific for LANA2

DATE-ISSUED: November 25, 2003

US-CL-CURRENT: 536/24.1, 424/199.1 , 424/229.1 , 435/325 , 435/91.1

APPL-NO: 09/ 733728

DATE FILED: December 8, 2000

US-PAT-NO: 6638504

DOCUMENT-IDENTIFIER: US 6638504 B1

TITLE: Methods for treating cancer

DATE-ISSUED: October 28, 2003

US-CL-CURRENT: 424/130.1, 435/4 , 435/7.1

APPL-NO: 09/ 298625

DATE FILED: April 23, 1999

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a Continuation-In-Part of U.S. Ser. No. 08/468,942 filed Jun. 6, 1995 now U.S. Pat. No. 5,965,360, which is a Divisional of U.S. Ser. No. 08/190,560 filed Jan. 31, 1994 now U.S. Pat. No. 5,798,257, which is a Continuation-In-Part of U.S. Ser. No. 07/981,455 filed Nov. 25, 1992 and now abandoned, which is a Rule 60 Continuation of U.S. Ser. No. 07/550,600 filed Jul. 9, 1990 now abandoned.

US-PAT-NO: 6630448

DOCUMENT-IDENTIFIER: US 6630448 B2

TITLE: Methods of inhibiting angiogenesis with endostatin protein

DATE-ISSUED: October 7, 2003

US-CL-CURRENT: 514/12, 514/2

APPL-NO: 09/ 154302

DATE FILED: September 16, 1998

PARENT-CASE:

CROSS REFERENCE TO PRIOR RELATED CASES

This application is a divisional application of U.S. patent application Ser. No. 08/740,168 filed Oct. 22, 1996, now U.S. Pat. No. 5,854,205 which claims priority to provisional application Serial No. 60/005,835 filed Oct. 23, 1995; provisional application Serial No. 60/023,070 filed Aug. 2, 1996; and provisional application Serial No. 60/026,263 filed Sep. 17, 1996. Each of the above-referenced applications is incorporated herein in its entirety.

US-PAT-NO: 6617114

DOCUMENT-IDENTIFIER: US 6617114 B1

TITLE: Identification of drug complementary combinatorial libraries

DATE-ISSUED: September 9, 2003

US-CL-CURRENT: 435/7.1, 435/4 , 435/5 , 435/6 , 435/DIG.14 , 435/DIG.2 , 435/DIG.27 , 435/DIG.9 , 530/324 , 530/325 , 530/330 , 530/350

APPL-NO: 09/ 069827

DATE FILED: April 30, 1998

PARENT-CASE:

This application is a continuation-in-part of Ser. No. 09/050,359, filed Mar. 31, 1998, which is a continuation-in-part of PCT/US97/19638, filed Oct. 31, 1997, which is a continuation-in-part of Ser. No. 08/740,671, filed Oct. 31, 1996, now abandoned, which applications are hereby incorporated by reference in their entirety.

US-PAT-NO: 6613883

DOCUMENT-IDENTIFIER: US 6613883 B1

TITLE: Screening assays for compounds that cause apoptosis and related compounds

DATE-ISSUED: September 2, 2003

US-CL-CURRENT: 530/358, 424/185.1 , 424/277.1 , 530/300 , 530/324 , 530/326 , 530/327 , 530/350

APPL-NO: 09/ 248776

DATE FILED: February 12, 1999

PARENT-CASE:

This application is a continuation of Ser. No. 08/675,631, filed Jul. 1, 1996, now U.S. Pat. No. 5,985,829 which is a continuation-in-part of U.S. application Ser. No. 08/359,316, filed on Dec. 19, 1994, now pending.

US-PAT-NO: 6607879

DOCUMENT-IDENTIFIER: US 6607879 B1

TITLE: Compositions for the detection of blood cell and immunological response gene expression

DATE-ISSUED: August 19, 2003

US-CL-CURRENT: 435/6, 435/69.1 , 536/23.1 , 536/24.1 , 536/24.3 , 536/24.31 , 536/24.32 , 536/24.33

APPL-NO: 09/ 023655

DATE FILED: February 9, 1998

US-PAT-NO: 6602979

DOCUMENT-IDENTIFIER: US 6602979 B1

TITLE: Screening assays for compounds that cause apoptosis

DATE-ISSUED: August 5, 2003

US-CL-CURRENT: 530/326, 530/350

APPL-NO: 08/ 359316

DATE FILED: December 19, 1994

US-PAT-NO: 6596506

DOCUMENT-IDENTIFIER: US 6596506 B2

TITLE: Double and triple readout assay systems

DATE-ISSUED: July 22, 2003

US-CL-CURRENT: 435/29, 435/320.1 , 435/325 , 435/366 , 435/6 , 435/7.21 , 435/8 , 536/24.1

APPL-NO: 09/ 999504

DATE FILED: October 25, 2001

PARENT-CASE:

RELATED APPLICATIONS

The present application claims priority to co-pending provisional application, U.S. Ser. No. 60/243,689, filed Oct. 27, 2000, which is incorporated herein by reference.

US-PAT-NO: 6586203

DOCUMENT-IDENTIFIER: US 6586203 B1

TITLE: ARF-P19, a novel regulator of the mammalian cell cycle

DATE-ISSUED: July 1, 2003

US-CL-CURRENT: 435/69.1, 514/12 , 514/2 , 514/44 , 530/350

APPL-NO: 09/ 129855

DATE FILED: August 6, 1998

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

The present Application is a Continuation-In-Part of U.S. Ser. No. 08/954,470 filed Oct. 20, 1993, now U.S. Pat. No. 5,876,965, issued Mar. 2, 1999 which is a Divisional of U.S. Ser. No. 08/534,975 filed on Sep. 27, 1995 now U.S. Pat. No. 5,723,313, issued Mar. 3, 1998, the disclosures of which are hereby incorporated by reference in their entireties. Applicants claim the benefit of these Applications under 35 U.S.C. .sctn.120.

PGPUB-DOCUMENT-NUMBER: 20030225025

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030225025 A1

TITLE: MDA-7 proteins and methods of use thereof

PUBLICATION-DATE: December 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fisher, Paul B.	Scarsdale	NY	US	
Jiang, Hongping	New York	NY	US	

APPL-NO: 10/ 417827

DATE FILED: April 17, 2003

RELATED-US-APPL-DATA:

child 10417827 A1 20030417

parent continuation-of 09221268 19981223 US PENDING

child 09221268 19981223 US

parent continuation-of 08316537 19940930 US GRANTED

parent-patent 6051376 US

child 08316537 19940930 US

parent continuation-in-part-of 08143576 19931027 US GRANTED

parent-patent 5643761 US

US-CL-CURRENT: 514/44, 435/6

ABSTRACT:

This invention provides a method of generating a subtracted cDNA library of a cell comprising: a) generating a cDNA library of the cell; b) isolating double-stranded DNAs from the cDNA library; c) releasing the double-stranded cDNA inserts from the double-stranded DNAs; d) denaturing the isolated double-stranded cDNA inserts; e) hybridizing the denatured double-stranded cDNA inserts with a labelled single-stranded nucleic acid molecules which are to be subtracted from the cDNA library; and f) separating the hybridized labeled single-stranded nucleic acid molecule from the double-stranded cDNA inserts, thereby generating a subtracted cDNA library of a cell. This invention also

provides different uses of the subtracted library.

[0001] This application is a continuation-in-part of U.S. application Ser. No. 08/143,576 filed Oct. 27, 1993, the contents of which are hereby incorporated by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (715):

[0756] Cell-cycle regulation results from the ordered activation of a series of related enzymes referred to as cyclin-dependent **kinases** (CDKs) (42). In normal cells, CDKs are predominantly found in multiple quaternary complexes, consisting of CDK, a cyclin, proliferating cell nuclear antigen (PCNA) and the p21 protein (43,44). p21 controls CDK activity, thereby affecting cell-cycle control and growth in mammalian cells (43-50). Using human glioblastoma cells containing an inducible wild-type **p53** tumor suppressor gene and subtraction hybridization, a gene called WAF1 (wild-type **p53-activated fragment** 1) that encodes an M.sub.r21,000 protein was identified (49,50). WAF1 is the same p21-encoding gene identified using the two-hybrid system as a potent CDK inhibitor, referred to as CPI1 (Cdk-interacting protein 1) (46). p.21 levels have been shown to increase in senescent cells (gene referred to as sdi-1; senescent cell-derived inhibitor) (51) and overexpression of p21 inhibits the growth of tumor cells (46,49,51). Treatment of wild-type **p53** containing cells with DNA damaging agents results in elevated wild-type **p53** protein and increased p21 levels (51). In this context, p21 may directly contribute to G.sub.1 growth arrest and apoptosis resulting in specific target cells after induction of DNA damage (51). Recent studies also demonstrate that p21 can: directly inhibit PCNA-dependent DNA replication in the absence of a cyclin/CDK; and inhibit the ability of PCNA to activate DNA polymerase .delta. by directly interacting with PCNA (52). These studies indicate that p21 is an important component of growth control, cell-cycle progression, DNA replication and the repair of damaged DNA.

Detail Description Paragraph - DETX (784):

[0823] The human p21 cyclin-dependent kinase (Cdk)-interacting protein CIP1 (Xiong et al., 1993b); Harper et al., 1993), and the mouse CAP20 homologue (Gu et al., 1993), is a ubiquitous inhibitor of cyclin kinases and an integral component of cell cycle control. This gene is identical to the WAF1 (wild-type (wt) p53 activated factor-1) gene identified following induction by wt **p53 protein expression in a human** glioblastoma multiforme cell line (El-Deiry et al., 1993). p21 has also been independently cloned as a consequence of induction of senescence in normal human foreskin fibroblast cells, SDI1 (senescent cell-derived inhibitor-1) (Noda et al., 1994), and during the process of terminal cell differentiation in human melanoma cells, mda-6 (Jiang and Fisher, 1993; Jiang et al., 1994). p21 is a nuclear localized protein that is inducted by DNA damage and during apoptosis in specific cell types as a function of wt p53 activation (El-Deiry et al., 1993, 1994). These studies suggest that p21 may be an important downstream mediator of wt p53-induced growth control in mammalian cells (El-Deiry et al., 1993, 1994). Somewhat paradoxical data indicates that WAF1/CIP1 is induced as an immediate-early gene

following mitogenic stimulation of growth arrested cells in a p53-independent manner (Michieli et al., 1994). Applicants presently demonstrate that mda-6 (WAF1/CIP1/SDI1) expression is also induced by mechanistically diverse acting agents resulting in macrophage/monocyte (TPA and Vit D3) or granulocyte (RA and DMSO) differentiation in human promyelocytic leukemia cells (Collins, 1987), HL-60, that lack endogenous p53 genes (Wolf and Rotter, 1985). Using differentiation-resistant variants (Homma et al., 1986; Mitchell et al., 1986), a direct correlation is found between the early induction of mda-6 expression and the onset of specific programs of differentiation in HL-60 cells. Applicants' results indicate that sustained p21 expression can be maintained in the absence of wt p53 protein and elevated levels of p21 (WAF1/CIP1/SDI1) mRNA and protein correlate with growth suppression and differentiation induction in a p53-independent manner in HL-60 cells.

Detail Description Paragraph - DETX (788):

[0826] To determine if the elevation in mda-6 expression with an increase in MDA-6 (WAF1/CIP1/SDI1) protein, HL-60 cells were labeled for 4 h with .sup.35S-methionine after 12, 24, 48 and 72 h treatment with TPA (3 nM), DMSO (1%) or RA (1 .mu.M) and lysates were immunoprecipitated using WAF1/CIP1 antibody (FIG. 28). As a control for protein loading, the level of ACTIN protein was determined by immunoprecipitation. Although no MDA-6 protein was detected in HL-60 cells, 12 h treatment with TPA or RA resulted in immunologically reactive MDA-6 protein. In 1% DMSO treated HL-60, MDA-6 protein was first apparent by 48 h. The levels of MDA-6 protein increased in a temporal manner with all three inducers and the highest levels were apparent at 72 h. The most active inducer of MDA-6 protein, as well as the most active growth suppressing agent, was TPA. Polyclonal antibodies prepared against **N-terminal peptide** regions of MDA-6 also immunoprecipitated MDA-6 from differentiation inducer treated HL-60 cells and human melanoma cells. In contrast, using a monoclonal antibody (PAb 421) that reacts with both wild-type and mutant **p53,** no reactive protein was detected after immunoprecipitation of .sup.35S-methionine labeled lysates prepared from HL-60 cells and TPA-, DMSO- or RA-treated HL-60 cells (data not shown). These results provide direct evidence that induction of elevated mda-6 mRNA expression in differentiation inducer-treated HL-60 cells results in elevated MDA-6 protein levels in the absence of **p53** protein.

Detail Description Paragraph - DETX (875):

[0908] Immunoprecipitation analysis of p53 under conditions preventing protein denaturization (<1% SDS) with monoclonal antibodies Ab1 (PAb421; Oncogene Sciences), that identifies both wild-type and mutant p53, and Ab3 (PAb240; Oncogene Sciences) that recognizes mutant p53, indicate that H0-1 cells contain a wild-type p53 protein (data not shown). A wild-type p53 protein is also present in a number of other cell types evaluated in the present study, including FM516-SV, L0-1, SH-1 and F0-1, whereas WM239 cells contain a mutant p53 (data not shown). To rule out potential artifacts, immunoprecipitation studies with Ab1 and Ab3 were performed with labeled extracts from cell lines with known p53 status, including MeWo (previously shown to contain a mutant p53 by sequence analysis) (Loganzo et al., 1994), Saos-2 (**p53-null phenotype), human** skin fibroblasts (wild-type p53) and SW480 colon carcinoma cells (mutant p53) (data not shown). The current results are

in agreement with several recent studies (Volkenandt et al., 1991; Castresana et al., 1993; Greenblatt et al., 1994; Montano et al., 1994; Loganzo et al., 1994) indicating that **p53 mutations are rare in human** melanoma and the majority of human melanomas contain a wild-type as opposed to a mutant p53 protein.

Detail Description Paragraph - DETX (876):

[0909] To determine the effect of the various inducing agents on **p53** and p21 protein levels the following experiment was performed. H0-1 cells were grown in inducer-free medium (control), IFN-.beta. (2000 units/ml), MEZ (10 ng/ml) or IFN-.beta.+MEZ (2000 units/ml+10 ng/ml) for 24, 48, 72 or 96 h, cells were labeled with .sup.35S-methionine and cell lysates were prepared and analyzed by immunoprecipitation analyses using Ab1 (PAb421), p21 (WAF1/CIP1, Santa Cruz Biotechnology; and rabbit polyclonal antibodies prepared against mda-6 **peptides**) and actin (Oncogene Sciences Inc.) (FIGS. 33 and 34). As observed with mRNA levels, no significant change in wild-type **p53** protein occurs in H0-1 cells treated for 24 h with IFN-.beta., MEZ or IFN-.beta.+MEZ (FIG. 33). In contrast, p21 mRNA and protein are induced in H0-1 cells, with IFN-.beta.+MEZ>MEZ>IFN-- .beta. (FIGS. 31A-E and 33). As seen with mRNA levels, the concentration of wild-type **p53** protein decreases and p21 protein increases over a 96 h period in MEZ and IFN-.beta.+MEZ treated H0-1 cells (FIG. 34). Increases in p21 protein are also seen in H0-1 cells treated with IFN-.beta. for 48, 72 or 96 h, whereas no change in wild-type **p53** protein occurs over the same period in similarly treated cells (FIG. 34). These results indicate that induction of p21 can occur without increases in wild-type **p53** protein (IFN-.beta. treated cells) and elevated levels of p21 under conditions of residual growth arrest and/or **terminal** differentiation correlate with a reduction in wild-type **p53** protein in H0-1 melanoma cells.

Detail Description Paragraph - DETX (886):

[0918] Metastatic human melanomas appear to be unique among **human cancers in their low frequency of p53** mutations and the prevalence of wild-type p53 protein in advanced cancers (Volkenandt et al., 1991; Castresana et al., 1993; Greenblatt et al., 1994; Montano et al., 1994; Lu & Kerbel, 1994). Studies by Loganzo et al. (1994) show that metastatic melanoma cells contain two- to 20-fold more p53 protein, in the majority of samples representing wild-type p53, than do melanocytes. Similarly, a large proportion of the human melanoma cell lines presently analyzed also contain wild-type p53 protein. In normal melanocytes, the level of mda-6 (p21) is higher than in metastatic melanomas, even though metastatic melanoma may contain more p53 (FIG. 35) (Loganzo et al., 1994). The increased level of p53 protein in melanoma cells appears to be a consequence of stabilization of the protein, i.e., the half-life is two- to five-fold greater than in melanocytes, irrespective of whether they contain wild-type or mutant-p53 (Loganzo et al., 1994). The stabilization of wt **p53 protein in human** melanoma cells does not result from the binding of this protein to either MDM2 or heat shock protein (Loganzo et al., 1994). The mechanism underlying this stabilization of wild-type p53 in metastatic melanomas is not presently known, but it might reflect a defective regulation of p53 that could allow these tumor cells to escape cell cycle arrest even in the presence of elevated p53. In fact, disturbances in **p53 expression are a common occurrence in human** melanomas and these abnormalities increase with

progression (for review see: Lu & Kerbel, 1994). These findings suggest that melanoma may represent a novel malignancy, in that it can coexist and evolve to more aggressive stages even in the presence of elevated levels of nuclear localized wt p53 protein. However, it is also possible that the wild-type **p53 protein in metastatic human** melanoma cells is functionally inactive (perhaps by interacting with other melanoma proteins) or the wild-type p53 protein is normal, i.e., can both bind and transcriptionally activate target genes, but the downstream genes normally responsive to wild-type **p53 are defective in metastatic human** melanoma. The inability of wild-type p53 to elevate mda-6 levels in metastatic melanoma, and consequently to induce proliferative control, could directly contribute to the increased instability of the evolving and progressing melanoma (Livingstone et al., 1992; Yin et al., 1992; Lu & Kerbel, 1994).

Detail Description Paragraph - DETX (888):

[0920] The present study provides additional evidence indicating that induction of p21 expression is independent of wild-type **p53 expression in human** melanoma cells. An interesting, yet somewhat paradoxical observation, is the temporal decrease in wild-type p53 protein with a corresponding increase in p21 protein during the process of growth arrest and induction of terminal differentiation in H0-1 melanoma cells (FIG. 34). In a number of cell culture model systems, p53 mRNA decreases as a function of growth suppression and the induction of differentiation (Shen et al., 1983; Mercer et al., 1984; Dony et al., 1985; Shobat et al., 1987; Khochbin et al., 1988; Richon et al., 1989; Hayes et al., 1991). Wild type p53 displays sequence-specific DNA-binding activity, sequence-specific transcriptional activation and induces growth suppression in a number of cell types, whereas all of these properties are lost in various mutant forms of the p53 protein (Ron, 1994; Pietenpol et al., 1994). The reduced levels of mda-6 (p21) in actively growing melanoma, even in the presence of high levels of wild type p53, and the elevations in p21 levels following wild type p53 suppression suggest that high levels of p21 expression may not be compatible with high levels of wild type **p53 in human** melanoma. This may occur because wild type p53 is inducing a downstream gene that may directly or indirectly modify p21 expression. The induction of growth arrest and terminal differentiation program by IFN-.beta.+MEZ in H0-1 cells may result in genotypic changes that mediate an inhibition of wild type p53 expression and consequently the absence of the downstream inhibitor of p21 expression. Alternatively, the wild type p53 protein that is present in metastatic melanoma may be functionally inactive or a downstream pathway modified by wild type p53 may be aberrant in progressing melanoma cells. In this context, the inverse relationship observed between wild type p53 and p21 protein levels may be associated with but not functionally relevant to growth arrest and terminal differentiation induced by MEZ and IFN-.beta.+MEZ.

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ABSTRACT:

The use of liposomal formulations, particularly formulations of positively charged and neutral lipids facilitates cellular uptake of SDI molecules. The transcription and/or expression of SDI-1-encoding nucleic acid molecules is facilitated by constructs that contain intervening untranslated regions.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of PCT US94/09700 (filed Aug. 26, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/274,535 (filed Jul. 13, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/229,420 (filed Apr. 15, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/203,535 (filed Feb. 25, 1994), which is a continuation-in-part of U.S. patent application Ser. No. 08/153,564 (filed Nov. 17, 1993) which is a continuation-in-part of U.S. patent application Ser. No. 08/113,372 (filed Aug. 30, 1993) which is a continuation-in-part of U.S. patent application Ser. No. 07/970,462 (filed Nov. 2, 1992, and issued as U.S. Pat. No. 5,302,706 on Apr. 12, 1994); and divisional U.S. patent application Ser. No. 08/160,814 (filed Jan. 3, 1994, pending) and Ser. No. 08/268,439 (filed Jun. 30, 1994); all of which Applications are continuations-in-part of U.S. patent application Ser. No. 07/808,523 (filed Dec. 16, 1991, now abandoned).

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Detail Description Paragraph - DETX (96):
[0147] Since p53 is an inducer of SDI expression, it, or a nucleic acid

encoding **p53, or biologically active fragments** of either, may be provided to cells in conjunction with an SDI molecule in order to obtain increased SDI expression.

Detail Description Paragraph - DETX (303):

[0330] Therefore, to demonstrate the direct induction of SDI-1 by p53, the above-described SDI-1 and antisense SDI-1 gene sequences were co-transfected with a **p53 gene construct into normal human** fibroblasts. As expected, the antisense construct was found to eliminate 80% of the inhibition of DNA synthesis caused by SDI-1 alone. When 4 .mu.g of SDI-1 and increasing amounts of p53 plasmids were co-transfected into MDAH 041 cells, the antisense SDI-1 was found to be capable of effectively counteracting the inhibition of DNA synthesis caused by p53 alone. These findings are summarized in Table 7. This finding verified the conclusion that one manner in which p53 causes inhibition of DNA synthesis is by activating the expression of SDI-1 and that such induction of SDI-1 is a requisite for part of the DNA synthesis-inhibitory activity of p53. Such activation occurs, at least in part, by the transcriptional activation of the SDI-1 gene. The expressed SDI-1 protein acts, in part, by inhibiting the kinase activities of CDK/cyclin complexes and can therefore act at multiple points in the cell cycle to block progression. Loss of wild type p53 activity would lead to lack of expression of SDI-1 and thereby result in inappropriate cell cycle progression.

Detail Description Paragraph - DETX (304):

[0331] Mutations in the gene encoding the **p53 protein are common in human** tumors with approximately 50% of tumors expressing a mutant p53. This has led to the conclusion that p53 acts as a negative growth regulator and is a tumor suppressor gene. One aspect of the present invention concerns the recognition of the molecular mechanism responsible for the anti-oncogene activity of p53. SDI-1 has been found to be an inhibitor of cell cycle progression which acts at least in part by inhibiting the kinase activities of cdk/cyclin complexes. As such it can act at multiple points in the cell cycle to block progression. Since p53 is required for transcriptional activation of SDI-1, inactivation of this function could allow uncontrolled and inappropriate cell cycle progression. This would allow cells to ignore the normal external signals for cell cycle stasis and permit proliferation in situ. Since SDI-1 is downstream of p53, SDI-1 appears to be the effector of p53 action. Furthermore, mutations have been found in SDI-1 which may contribute to altered cell proliferation in cells without mutated p53.

Detail Description Paragraph - DETX (409):

[0410] Recent reports suggest that CPT may alter p34.sup.cdc2/cyclin B complex regulation in HeLa cells (Tsao, Y. P. et al., Canc. Res. 52:1823-1829 (1992)) and induce wild type **p53** protein in ML-1 myeloid leukemia cells and in LNCaP prostatic adenocarcinoma cells (Nelson, W. G. et al., Molec. Cell. Biol. 14:1815-1823 (1994)). Significantly, both events appear to require active DNA synthesis. In this context, it has been reported that **p53** may activate wild type **p53-activated fragment** 1, SDI-1 (sometimes referred to as Waf-1) El-Deiry, W. S. et al., Cell 75:805-816 (1993)). As indicated above, SDI-1 plays a critical role in the regulation of cell growth in tumor and

senescent cells by inhibiting cyclin-dependent **kinases** and by subsequently interrupting the cell division process. To expand these observations and to gain insight into the molecular mechanism of CPT-induced cytostasis, the expression of SDI-1 was evaluated in non-tumorigenic cells and the results were correlated with those from studies examining the effects of CPT on cell proliferation and metabolic activity, DNA synthesis, and perturbation in the cell cycle.

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PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a Continuation-In-Part of U.S. Ser. No. 08/468,942 filed Jun. 6, 1995 now U.S. Pat. No. 5,965,360, which is a Divisional of U.S. Ser. No. 08/190,560 filed Jan. 31, 1994 now U.S. Pat. No. 5,798,257, which is a Continuation-In-Part of U.S. Ser. No. 07/981,455 filed Nov. 25, 1992 and now abandoned, which is a Rule 60 Continuation of U.S. Ser. No. 07/550,600 filed Jul. 9, 1990 now abandoned.

US-CL-CURRENT: 424/130.1, 435/4 , 435/7.1

ABSTRACT:

The present invention is directed towards the diagnosis of malignant cancer by detection of the mts-1 MRNA or the mts-1 protein, encoded by the mts-1 gene. The present invention contemplates the use of recombinant mts-1 DNA and antibodies directed against the mts-1 protein to diagnose the metastatic potential of several types of tumor cells, including, for example, thyroid, epithelial, lung, liver and kidney tumor cells. The present invention is also directed to mammalian cell lines and tumors with high and low metastatic potential which have been developed to serve as tseful model systems for in vitro and in vivo anti-metastasis drug screening.

5 Claims, 46 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 33

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Brief Summary Text - BSTX (12):

The nucleotide and amino acid sequences of **human p53** have been reported by Zakut-Houri et al, EMBO J. 4: 1251-1255, 1985). The ability of p53 to bind DNA in a sequence-specific manner maps to amino acid residues 90-290 of **human p53** (Pavletich et al, Genes Dev. 7: 2556-2564, 1993; and Wang et al, Genes Dev. 7: 2575-2586 1993); the tetramerization domain maps to amino acid residues 322-355 of **human p53**. The DNA binding-regulation domain maps to amino acid residues 364-393 of **human p53** or to the corresponding region encompassing residues 361-390 of mouse p53 (Hupp et al., Cell 71: 875-886, 1992; and Halazonetis et al., EMBO J. 12: 1021-1028, 1993).

Brief Summary Text - BSTX (13):

Inactivation of **p53 is associated with more than half of all human** tumors. The inactivation can occur by mutation of the p53 gene or through binding of p53 to viral or cellular oncogene proteins, such as the SV40 large T antigen and MDM2. Mutations of the **p53 protein in most human** tumors involve the sequence-specific DNA binding domain (Bargonetti et al., Genes Dev. 6: 1886-1898, 1992).

Brief Summary Text - BSTX (24):

Another embodiment of the present invention provides a method for intercepting the binding between **p53** and Mts-1 in a subject by administering to the subject, an effective amount of a **peptide which prevents the interaction between p53** and Mts-1 by binding to Mts-1. For example, one such **peptide comprises the C-terminal region of p53** (amino acid 289-393 of **human p53** or amino acid 289-390 of murine **p53**), in particular, amino acid 360-393 of **human p53** or amino acid 360-390 of murine **p53**. Functional **fragments** or analogs of such **peptides** are also within the scope of the present invention. Another example of a binding-intercepting **peptide** comprises amino acid 1909-1937 of non-muscle myosin heavy chain or functional **fragments** of analogs thereof.

Brief Summary Text - BSTX (25):

In one embodiment, the present invention provides methods of treating a tumor in a subject by administering to the subject, a therapeutically effective amount of a nucleic acid molecule coding for a **peptide which prevents the binding of Mts-1 to p53**.

Brief Summary Text - BSTX (26):

In one embodiment, the present invention provides methods of treating a tumor in a subject by administering to the subject, a therapeutically effective amount of a **peptide which prevents the binding of Mts-1 to p53**.

Drawing Description Text - DRTX (35):

FIG. 21 depicts Mts1 interaction with target proteins in a blot-overlay assay. Recombinant full size **p53** (1), N-**terminal** domain (2), DNA-binding domain (3), C-**terminal** domain (4) and the **fragment** of the non-muscle myosin (5)

after gel electrophoresis were transferred onto nitrocellulose membrane. Identical membranes were incubated with different batches of the recombinant Mts1 protein (Mts1-a, Mts1-b, Mts1-c and Mts1-d). Mts1 bound to the fixed proteins was detected by the anti-Mts1 serum. The graph at the upper left depicts the schematic localization of the proteins on the membranes.

Detailed Description Text - DETX (70):

The present invention provides **peptides which prevent p53 from binding to Mts1, e.g., a peptide comprising aa 289-393 of human p53, a peptide comprising aa 360-393 of human p53, a peptide comprising aa 289-390 of murine p53, a peptide comprising aa 360-390 of murine p53, a peptide** comprising the C-**terminal** nonmuscle myosin heavy chain, a **peptide** comprising amino acid 1909-1937 of human nonmuscle myosin heavy chain. Functional **fragments** and analogs of these **peptides** are also contemplated by the present invention.

Detailed Description Text - DETX (71):

"Functional fragments" refer to peptide fragments that have the same function as the **peptide in issue, namely, the function of interfering the Mts1-p53** interaction by binding to Mts-1.

Detailed Description Text - DETX (72):

By "analogs" it means variants of a peptide in issue. The variations include substitutions, insertions or deletions of one or more amino acid residues, or modifications of the side chains of the amino acid residues. Thus, analogs of a peptide can include homologous peptides from other mammalian species, peptides containing non-natural amino acid residues, peptides having chemical modifications on the side groups of amino acid residues, as well as peptides artificially designed to resemble the three dimensional structure of the binding site on **human p53**.

Detailed Description Text - DETX (73):

A variety of techniques are available to those skilled in the art to make various **fragments or analogs of p53**. Such techniques include standard chemical synthesis, recombinant expression, and structural modeling (also called `mimetics`). The sequences of p53 from a number of mammalian species are highly conserved and are available to those skilled in the art, e.g., via Databases such as GenBank.

Detailed Description Text - DETX (78):

The present invention also contemplates pharmaceutical compositions which include, as an active ingredient, an Mts1-**p53 binding intercepting peptide** as described hereinabove, and a pharmaceutically acceptable carrier.

Detailed Description Text - DETX (79):

In another aspect of the present invention, Mts1-**p53 binding-intercepting peptides** or nucleic acid molecules encoding thereof are used for treating

tumors.

Detailed Description Text - DETX (84):
In one embodiment, the present invention provides methods of treating a tumor in a subject by administering to the subject, a therapeutically effective amount of a **peptide which prevents the binding of Mts-1 to p53**. Preferred binding intercepting peptides have been described hereinabove.

Detailed Description Text - DETX (85):
In another embodiment, the present invention provides methods of treating a tumor in a subject by administering to the subject, a therapeutically effective amount of a nucleic acid molecule coding for a **peptide which prevents the binding of Mts-1 to p53**.

Detailed Description Text - DETX (253):
The following mouse wild type p53 PCRs were designed: #1--full size coding region (390 aa) was amplified using primers: forward CGGGATCCGACTGGATGACTGCCATGGA (SEQ ID NO:10) (having a BamHI site), reverse CGAAGCTTCAGTCTGAGTCAGGCCCCACT (SEQ ID NO:11) (including a HindIII site); #2--N-terminal domain (106 aa): forward, same as the forward primer for #1, and reverse CGAAGTCTTGAAGCCATAGTTGCCCTGGTAAG (SEQ ID NO:12)(including a HindIII site); #3--DNA-binding domain (185 aa) : forward CGGGATCCCACCTGGGCTTCCTGCATGCT (SEQ ID NO:13) (including a BamHI site), reverse CGAAGCTTGGACTTCCTTTTTTGCGGAAATTTTC (SEQ ID NO:14) (including a HindIII site); #4--C-terminal (99 aa): forward CGGGATCCCTTTGCCCTGAACTGCCCCCA (SEQ ID NO:15) (including a BamHI site), and reverse--same as the reverse primer for #1. The PCR products were digested with BamHI/HindIII and cloned in eukaryotic expression vector pXmyctag, containing a CMV promoter and 8-aa myc tag, and bacterial expression vector pQE30 (Qiagen). PSP65m65 plasmid DNA was used for the amplification of p53. Human pC53-SN3 (**human wild type p53) and pC53-SCX3 (human mutant Human mutant p53**-pC53-SCX3 (143.sup.Val-Ala) eukaryotic expression plasmids were obtained. For conditional expression, mts1 cDNA was excised, cloned in pUHD 10-3 and used for transfection of cell lines producing reverse tetracycline-controlled transactivator (pUHD172-neo) (Clontech).

Detailed Description Text - DETX (264):
For in vitro pull down assay, 1 .mu.g recombinant Mts1 was mixed with recombinant full size **p53 and its domain peptides** in 150 mM NaCl-50 mM Tris-HCl pH 8.0-0.5% NP-40 and precleaned on Protein A-Sepharose on the presence of protease inhibitors at 1 hour in cold room. To the precleaned mixtures, fresh **portions of the protein A-sepharose and the corresponding anti-p53** antibodies were added: pAb421 for full-size and C**-terminal** domain, pAb240 for DNA-binding core domain and E-19 for the N**-terminal** domain, and incubated for 2 hours in the cold room. Following 5 washes, immunoprecipitates were denaturated by heating at 100.degree. C.-5 min, separated in 15% PAAG and transferred to Immobilon-P (Millipore). To detect the co-immunoprecipitated Mts1 protein, membranes were probed with anti-Mts1 antibody and developed by the ECL System. Recombinant **human wild type GST-p53** and GST**-p53**-.DELTA.30 (deletion mutant

lacking amino acid residues 364-393) fusion proteins were used for pull down experiments with the Mts1 recombinant protein. 5 .mu.g of GST and GST-fusion proteins coupled with Glutathione-sepharose beads were incubated with 2 .mu.g of the Mts1 protein in NP-40 buffer (1% NP-40, 50 mM Tris-HCl pH 8.0-150 mM NaCl) for 2 h in the cold room with rotation. Beads with proteins bound were washed 5 times with NP-40-buffer. Proteins were isolated by boiling in the protein loading buffer for 5 min and analyzed using Western blotting.

Detailed Description Text - DETX (266):

Reactions were performed in a mixture (2 .mu.l) containing 50 mM Tris-HCl pH 7.6, 0.2 M NaCl, 10 mM MgCl.sub.2, 4 mM CaCl.sub.2, 2 mM dithiothreitol, 15 .mu.l ATP (Amersham Pharmacia Biotech), 25 .mu.Ci [.gamma.-.sup.32 P]-ATP (5000 Ci/nnol, Amersham Pharmacia Biotech), 1 .mu.M recombinant wild type **p53 or this protein fragments** for 30 min at 30.degree. C. PKC assay was done in the presence of 7.5 .mu.g of phosphatidylserine (Sigma) by 0.025 .mu.g PKC (Roche). CKII was purchased from New England BioLabs Inc., and 50 units were applied per each reaction. Recombinant Mts1 was sued in concentrations of 3,5 and 9 .mu.M reactions were **terminated** by 15% SDS-PAGE. Gels were fixed in 10% trichloracetic acid, dried and exposed to Kodak x-ray film.

Detailed Description Text - DETX (278):

Another approach, Far-Western blot analysis, was also employed to assess the interaction between Mts1 and **p53**. Full size **p53** and its functional domains, expressed in E.coli, were separated on SDS-PAGE and transferred into Immobilon-P. Filters were incubated with recombinant Mts1 in conditions allowing the interaction with the proteins fixed on the membrane. Mts1 bound to **p53** proteins on the filter, was detected with anti-Mts1 antibody. Data shown in FIG. 21, consistent with the IP results, indicated that Mts1 was able to bind full-size **p53** and its C**-terminal** domain. As a positive control we have used recombinant **fragment** of non-muscle myosin which is known as a target for Mts1 protein (FIG. 21, lane 5). BSA loaded in 5.times. excess did not reveal nonspecific mts1 binding in Far-Western assay, neither did N**-terminal** or DNA-binding domains.

Detailed Description Text - DETX (282):

As shown in FIG. 22, Mts-1 inhibited the **phosphorylation** of full-size **p53 and the C-terminal protein fragment** by PKC. Addition of the same concentrations of Mts1 to the PKC reaction mixture did not affect the **phosphorylation** of the N**-terminal** and DNA-binding domains of **p53**. No interference of Mts1 was shown with CK II **phosphorylation of p53** and its domains (FIG. 23). These observations indicate that Mts1 specifically inhibited the **phosphorylation** of PKC of the C**-terminal** domain of **p53**.

Other Reference Publication - OREF (16):

Wilder, P.T., et al. (1996) (Abstract) "S100.beta. Inhibition of PKC.alpha. And PKM Phosphorylaion of a Synthetic **Peptide Derived From p53.**", Biophys.J 70:A62.

Other Reference Publication - OREF (17):

Wilder, P.T., et al. (1998) "S100B (.beta..beta.) inhibits the protein **kinase** C-dependent **phosphorylation of a peptide derived from p53** in a Ca.sup.2+ -dependent manner", Protein Science 7:794-798.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	135	dna adj (pk or activated adj (protein adj kinase$1 or pk))	USPAT; US-PGPUB	2004/01/06 10:35
2	L2	43	1 same (substrate$ or peptide$)	USPAT; US-PGPUB	2004/01/06 10:41
3	L3	27	1 same (assay$8 or detect$8 or quantit$8)	USPAT; US-PGPUB	2004/01/06 10:46
4	L5	8136	p53	USPAT; US-PGPUB	2004/01/06 10:49
5	L6	622	5 near6 (fragment$4 or peptide$ or portion$)	USPAT; US-PGPUB	2004/01/06 10:49
6	L7	1213	5 near4 human	USPAT; US-PGPUB	2004/01/06 10:49
7	L8	332	6 and 7	USPAT; US-PGPUB	2004/01/06 10:49
8	L9	651	5 same (phosphorylat$ or kinase$1 or termin$8) same (fragment$4 or peptide$ or portion$)	USPAT; US-PGPUB	2004/01/06 10:50
9	L10	153	8 and 9	USPAT; US-PGPUB	2004/01/06 10:50
10	L11	20	6 and 1	USPAT; US-PGPUB	2004/01/06 11:45

PGPUB-DOCUMENT-NUMBER: 20030228675

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030228675 A1

TITLE: ATM related kinase ATX, nucleic acids encoding same and methods of use

PUBLICATION-DATE: December 11, 2003

US-CL-CURRENT: 435/199, 435/320.1 , 435/325 , 435/69.1 , 514/263.3 , 536/23.2

APPL-NO: 10/ 165216

DATE FILED: June 6, 2002

PGPUB-DOCUMENT-NUMBER: 20030203407

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030203407 A1

TITLE: Compositions and methods for monitoring the phosphorylation of natural binding partners

PUBLICATION-DATE: October 30, 2003

US-CL-CURRENT: 435/7.1, 530/388.26

APPL-NO: 10/ 382017

DATE FILED: March 5, 2003

RELATED-US-APPL-DATA:

child 10382017 A1 20030305

parent division-of 09511204 20000223 US PENDING

child 09511204 20000223 US

parent continuation-in-part-of 09258981 19990226 US PENDING

PGPUB-DOCUMENT-NUMBER: 20030176373

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030176373 A1

TITLE: Agents that modulate DNA-PK activity and methods of use thereof

PUBLICATION-DATE: September 18, 2003

US-CL-CURRENT: 514/44, 435/455 , 435/6

APPL-NO: 09/ 848986

DATE FILED: May 4, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60202274 20000505 US

non-provisional-of-provisional 60262321 20010117 US

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application serial No. 60/202,274, filed May 5, 2000, and U.S. Provisional Application serial No. 60/262,321, filed Jan. 17, 2001, both of which are incorporated by reference herein in their entirety.

PGPUB-DOCUMENT-NUMBER: 20030162237

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162237 A1

TITLE: Methods of monitoring enzyme activity

PUBLICATION-DATE: August 28, 2003

US-CL-CURRENT: 435/7.92, 435/6

APPL-NO: 10/ 308967

DATE FILED: December 3, 2002

RELATED-US-APPL-DATA:

child 10308967 A1 20021203

parent continuation-in-part-of PCT/GB01/02502 20010607 US UNKNOWN

non-provisional-of-provisional 60211313 20000613 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
GB	0013888.3	2000GB-0013888.3	June 7, 2000

PGPUB-DOCUMENT-NUMBER: 20030157572

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030157572 A1

TITLE: ATM kinase compositions and methods

PUBLICATION-DATE: August 21, 2003

US-CL-CURRENT: 435/7.2, 435/194 , 435/7.92

APPL-NO: 10/ 351733

DATE FILED: January 24, 2003

RELATED-US-APPL-DATA:

child 10351733 A1 20030124

parent continuation-in-part-of 10307077 20021127 US PENDING

INTRODUCTION

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 10/307,077, filed Nov. 27, 2002 which is incorporated herein by reference in its entirety.

PGPUB-DOCUMENT-NUMBER: 20030125284

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030125284 A1

TITLE: Agents that modulate DNA-PK activity and methods of use thereof

PUBLICATION-DATE: July 3, 2003

US-CL-CURRENT: 514/44, 435/6

APPL-NO: 10/ 233121

DATE FILED: August 30, 2002

RELATED-US-APPL-DATA:

child 10233121 A1 20020830

parent division-of 09848986 20010504 US PENDING

non-provisional-of-provisional 60202274 20000505 US

non-provisional-of-provisional 60262321 20010117 US

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application serial No. 60/202,274, filed May 5, 2000, and U.S. Provisional Application serial No. 60/262,321, filed Jan. 17, 2001, both of which are incorporated by reference herein in their entirety.

US-PAT-NO: 6670144

DOCUMENT-IDENTIFIER: US 6670144 B1

TITLE: Compositions and methods for monitoring the phosphorylation of natural binding partners

DATE-ISSUED: December 30, 2003

US-CL-CURRENT: 435/21, 435/183 , 435/188 , 435/188.5 , 435/194 , 435/7.8 , 435/7.9 , 435/7.91

APPL-NO: 09/ 511204

DATE FILED: February 23, 2000

PARENT-CASE:

This application is a continuation-in-part of application Ser. No. 09/258,981, filed Feb. 26, 1999.

US-PAT-NO: 6656696

DOCUMENT-IDENTIFIER: US 6656696 B2

TITLE: Compositions and methods for monitoring the phosphorylation of natural binding partners

DATE-ISSUED: December 2, 2003

US-CL-CURRENT: 435/7.6, 435/188 , 435/21 , 435/7.1 , 435/7.4 , 435/7.7 , 435/7.71 , 435/7.72 , 435/7.9 , 436/537 , 436/544 , 436/546 , 536/25.32

APPL-NO: 09/ 258981

DATE FILED: February 26, 1999